

**GASTRO-INTESTINAL INFECTION IN RELATION TO INFECTION OF THE LIVER AND BILE PASSAGES**

(A Continuation).

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**Résumé of Former Report.** In 1916 the patient first appeared, suffering from debility, hypochlorhydria and lowered nutrition; there were no symptoms related to the liver or to the intestine. She was discharged eight weeks later, showing general improvement, and was in good health until the spring of 1919, when there developed intractable diarrhea. She returned to Buffalo in September, 1919, with gastro-enterocolitis of the greatest intensity in the small intestine and with gas bacilli and streptococci abundant. The stomach showed atonic dilatation, achylia, pus cells, red blood cells and an excess of mucus. In November, 1919, the diarrhea was controlled, gastric secretion reappeared and the patient was discharged, taking a smooth diet. Improvement continued for a month, with a gain in weight of fourteen pounds, but she ate too freely and became for the first time jaundiced. On December 24, three weeks later, she came again to Buffalo. There was complete associated jaundice, with acholic stools. A study of the stomach and duodenal contents indicated severe duodenitis. There was a recurrence of diarrhea. The liver was enlarged and slightly tender to pressure, but there was no pain.

**Conclusion.** Biliary obstruction from swelling at the ampulla of Vater.

There was slight elevation of temperature and a leukocyte count of 6100. Duodenal lavage was practised with benefit. The jaundice diminished, became intermittent with occasional rigors, followed by fever and renewed jaundice with leukocytosis. The clinical picture corresponded with the old conceptions of angiocholitis. The intestine, including the colon, showed atony and catarrhal inflammation. Under deep duodenal feeding, duodenal lavage and colonic irrigations the patient improved. In May, 1920, recovery seemed possible, as stated at our last meeting.\*

**History of the Case as Developed Subsequent to the Report Made at the Last Meeting of the Association.** The patient had almost invariably a good appetite. At times there was slight gastric secretion (hypochlorhydria), at other times secretion was absent, with evidence of a low-grade gastritis. Intermittently the stools showed bile coloring matter and bile salts, but not always associated. She was not studied as to the presence of hemoconias.

\* Transactions, twenty-third Annual Session of the American Gastro-Enterological Association, May 3 and 4, 1920. See "Annals of Medicine," vol. 1, No. 2.

In the duodenal contents pancreatic ferments were very deficient. There was feeble amyolytic enzyme, still feebler proteolytic enzyme and usually absence of lipase action. Always there was mucus in excess, occurring often in shreds, containing numerous pus cells, at times many degenerated red blood cells.

It was evident that there was an open passage through the bile ducts, but nevertheless infection coming through the biliary channels. This was proved by the use of the duodenal tube after irrigation of the stomach and duodenum. It was also evident that there was a very defective digestive power in the duodenum as result of the disordered pancreas and the duodenitis. At this time the suggestion was made by Dr. Rose Donk, who was assisting on the case, that the transfusion of normal duodenal contents from a healthy donor might provide the patient with needed digestive ferments and help her to gain in nutrition. This treatment was carried out by Dr. Donk under my observation during a period of two weeks. The healthy donor while fasting, having had passed the duodenal tube and having had the secretions stimulated by small quantities of hot water, gave out from 60 to 200 cc of duodenal contents, which were immediately introduced through a tube into the duodenum of the patient. The result of this treatment was published by Dr. Donk,<sup>2</sup> under the title "Transfusion of Duodenal Contents." The work was interesting, and unquestionably the patient received temporary benefit from the measure. I am convinced that this suggestion made by Dr. Donk will prove to be of some practical importance in selected cases.

Intestinal perfusion was also practised at other times, with apparent benefit. A freer flow of bile was promoted by irrigation with magnesium sulphate solution as suggested by Meltzer. The diarrhea never recurred with its former intensity, yet there was a continued predisposition to looseness requiring attention and at times special medication. The sigmoidoscope revealed a catarrhal colitis but no bleeding-points. The patient in February had a definite intestinal hemorrhage unexplained in origin.

Medical and surgical consultants leaned to the opinion that there was more trouble in the gall-bladder than had been hitherto believed. It was suggested that we were dealing with a chronic cholecystitis with calculi. There was no evidence of this, however, in the radiograms which were shown and discussed at our last meeting. To my mind it seemed clear that the trouble was not from the gall-bladder, but that we had, following the blocking at the papilla in the beginning of the jaundice, an ascending infection which reached the liver and probably the pancreas.

During May the case was at a standstill, with an occasional discouraging relapse; that is, chills, fever and leukocytosis, the

<sup>2</sup> Jour. Am. Med. Assn., November 13, 1920.

attack lasting two or three days; then the jaundice would fade, but it never disappeared. It was decided, finally, that there should be made a cholecystostomy, with the hope that by removing a cholecystitis the infection passing into the intestine would be eliminated and that the patient might be benefited. Also, it would settle the question as to calculi.

The operation was made under gas and ether anesthesia, which was preceded by a transfusion of 750 cc of blood from a well-typed donor. The transfusion was intended not only to strengthen the patient but to increase the coagulability of the blood, which had been found to be fourteen minutes plus. Following the transfusion, Dr. James A. MacLeod operated upon the patient, removing the appendix, which showed chronic inflammation, and performing cholecystostomy. It was decided to do little exploring, so that the shock might be at the minimum. However, it was found that there was no evidence of tumor about the stomach or duodenum; the pancreas was unusually firm on palpation; the gall-bladder was not distended but was rather pale, and contained no calculi, but a small amount of rather dark bile of increased consistency. The liver was apparently moderately enlarged, pale yellow in color, rather firm upon palpation, with the surface irregular as seen in cirrhosis. The common duct was not explored.

The patient endured the operation remarkably well and seemed to be in better condition after it than before, doubtless from the transfusion. The amount of bile drainage was small and we felt that little was directly gained by the operation. For some days, however, the patient did well, when there ensued another, and this time severe, intestinal hemorrhage, and transfusion seemed necessary to save life; 500 cc of blood were therefore introduced into a vein. The blood was taken from a new donor. There was no agglutination shown on typing, but subsequently it was found that the patient's serum hemolyzed the donor's corpuscles. There followed great prostration, with unconsciousness. In the state of depression, amounting almost to shock, which followed the second transfusion with blood, there appeared in the urine a large amount of urobilin. Previously it never had appeared in the urine, and after that event it never disappeared. It is an interesting question as to what effect this transfusion may have had upon the liver to hasten its degeneration in its already crippled and infected state. There is, of course, the possibility of coincidence, but the clinical fact remains striking. For a few days it looked as though the patient would succumb from hemolysis and protein-poisoning. However, she rallied and matters progressed favorably for a few days, although there continued to be marked urobilinuria. At this time drainage of bile was insignificant, and it occurred to me that benefit might follow irrigation of the gall-bladder through the drainage tube, with a magnesium sulphate solution of 25 per

cent. This was practised, with the result that the drainage of dark-colored bile was much increased. There was considerable diminution of the jaundice, which had deepened since the operation. I think that real but transient improvement followed this irrigation of the gall-bladder with a magnesium sulphate solution. This was carried out for a month, the patient making slow improvement. The evidences of infection were less conspicuous—that is to say, there was absence of chills, but a slight temperature. Under the treatment the liver shrank in size and it was difficult to keep a drainage tube in place for purposes of irrigation. Finally, irrigation became impossible, the wound healed and the patient was sent to her home.

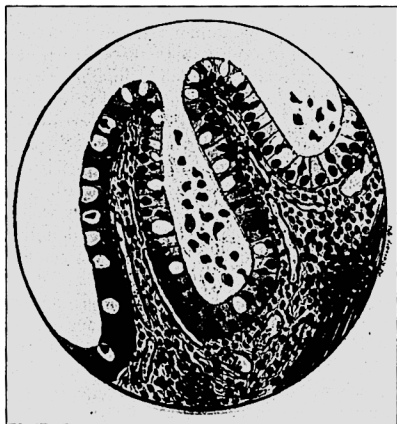


FIG. 1.—High-power sketch of intestine with two villi. Numerous goblet cells among the surface epithelial cells, leukocytes free between the villi and migrating through the epithelium; dilated capillaries, cell collection in the submucosa, all indicating subacute enteritis.

She made the journey of one hundred and fifty miles with little difficulty, and continued with but little change in her condition for about a month, when she somewhat suddenly went into a collapse and died.

Dr. William F. Jacobs, pathologist, accompanied me to her home and there was made a careful but incomplete autopsy, limited to the examination of the abdominal viscera. The results of this postmortem study were interesting. The stomach showed dilatation with gastritis. From the gross appearance the mucous tissues of the duodenum were infiltrated, swollen, intensely red and some-

what softened. This catarrhal state of the intestine was observed throughout the gut, being less evident in the colon than in the small intestine, and more marked in the duodenum than elsewhere. There were no adhesions from the appendectomy. There were the usual adhesions at the site of the duodenostomy. From microscopic sections the tunics of the stomach and intestine showed less inflammatory change than would have been anticipated from their appearance, yet on microscopic section marked duodenitis was demonstrated. The gall-bladder was contracted but showed no growth on culture. The biliary passages, including the common duct, cystic duct and hepatic duct, were healthy. There was no evidence of calculus past or present, nor was there evidence of past cholangitis.

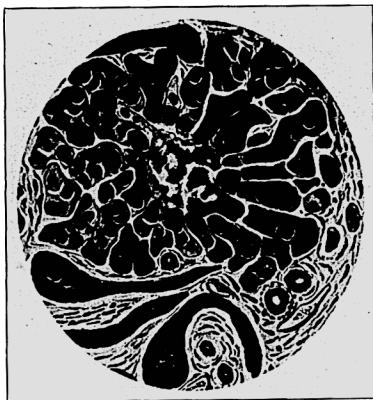


FIG. 2.—High-power diagrammatic sketch of part of a liver lobule, with small central area of necrosis and new-forming bile ducts at the edge.

The striking and interesting features of the case were found in the structures of the liver itself. This organ had shrunk to perhaps two-thirds its normal volume, which it will be recalled was large during the six months preceding the operation, and also at that time. It was yellowish, fawn-colored, with small irregularities of surface, such as one sees in hepatic cirrhosis. On incision of the liver in all parts of the organ there were found countless areas of necrosis, rather dry in character, containing débris. The tissues presented the picture of minute areas of hepatitis, in which the biliary passages escaped except at their origin, as occurs in biliary cirrhosis. There was marked ingrowth of connective tissue

containing many new-formed bile ducts. The pancreas showed but slight interstitial change; there was no evidence of actual infection.

From a strictly postmortem point of view it might seem that the process had begun in the liver and that the bile had led to infection of the intestinal tract. Such a conclusion does not correspond with the history of the case. It will be recalled that the patient suffered primarily from gastritis and failing gastric function, and three years later from enteritis, and was subsequently never free from these conditions. There was no jaundice preceding the last eight months of life. It is my own judgment (and I think the morbid

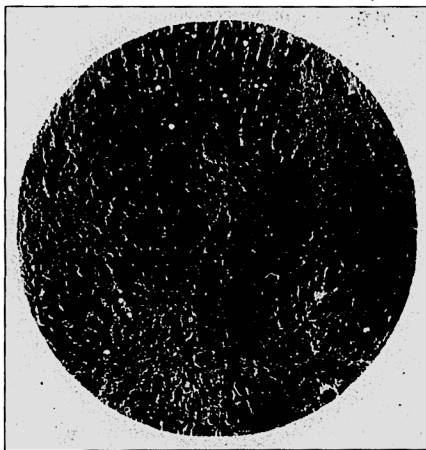


FIG. 3.—Quite low-power photomicrograph of the liver. An area of well-stained liver tissue shading into unstained and necrotic tissue. Also cellular fibrous tissue with bile ducts.

structures support this view) that the disease was primarily a gastritis, later an intense duodenitis; that there was from swelling of the duodenal mucosa, a blocking at the papilla, which caused the first attack of jaundice. Meantime infection had been carried to the liver through the portal system, and thus there was set up a hepatitis with descending inflammation, and not one that ascended through the biliary tract, as I had naturally inferred. I feel that this statement is worthy of repetition and emphasis, for the reason that this case seems to illustrate the growing belief that jaundice is more often the result of an infective or toxic hepatitis, with the infection descending, than an ascending infection; that is to say,

the infection reaches the liver through the portal system, and the obstruction to the outflowing bile occurs in and about the lobules and possibly at the beginning biliary passages. This is not to deny the well-known fact that jaundice often arises from obstruction at the common duct or the hepatic duct, and this obstruction may, of course, be inflammatory. Except in the instance of calculi causing actual obstruction at the junction of the cystic and common ducts or in the ampulla, jaundice is probably rather rare from simple angiocholitis of ascending nature.

There are the following outstanding features to the history of the case:

1. The relationship that may exist between hepatitis with necrotic areas, later replaced by interstitial ingrowth on the one hand, and on the other hand persistent gastro-enterocolitis, in some regions intense.

2. With this pathology, nevertheless, there was escape from involvement or inflammation of the chief bile channels and the gall-bladder, as shown during life by operation and later by post-mortem.

3. The illustration of possibly beneficial results from a novel method of treatment, that of transfusion of the normal duodenal content of a healthy donor into the functionless duodenum of a patient, also the value of intestinal perfusion.

4. The remarkable effect in stimulating the flow of bile from a badly diseased liver by direct irrigation of the gall-bladder with a magnesium sulphate solution. This also is, so far as I know, a novel measure of treatment, and is interesting to compare with the method of stimulating the outflow of bile as described by Vincent Lyon.

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#### **CALCIFICATION OF THE PITUITARY WITH HYPOPITUITARISM AND WITH SYMPTOMATIC TREATMENT.\***

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AND

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It has been said by someone that the pituitary is the "gland of personality." To this might be added "It is the gland of romance." Not only has it a great deal to do with physical and mental vigor, the stature, form, color and amount of hair, sex characteristics and physical strength, all being controlled by this bean-sized organ

\* Read before the Section on General Medicine, College of Physicians, Philadelphia, May 30, 1921.